

WO 99/42481

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PCT/DE99/00554

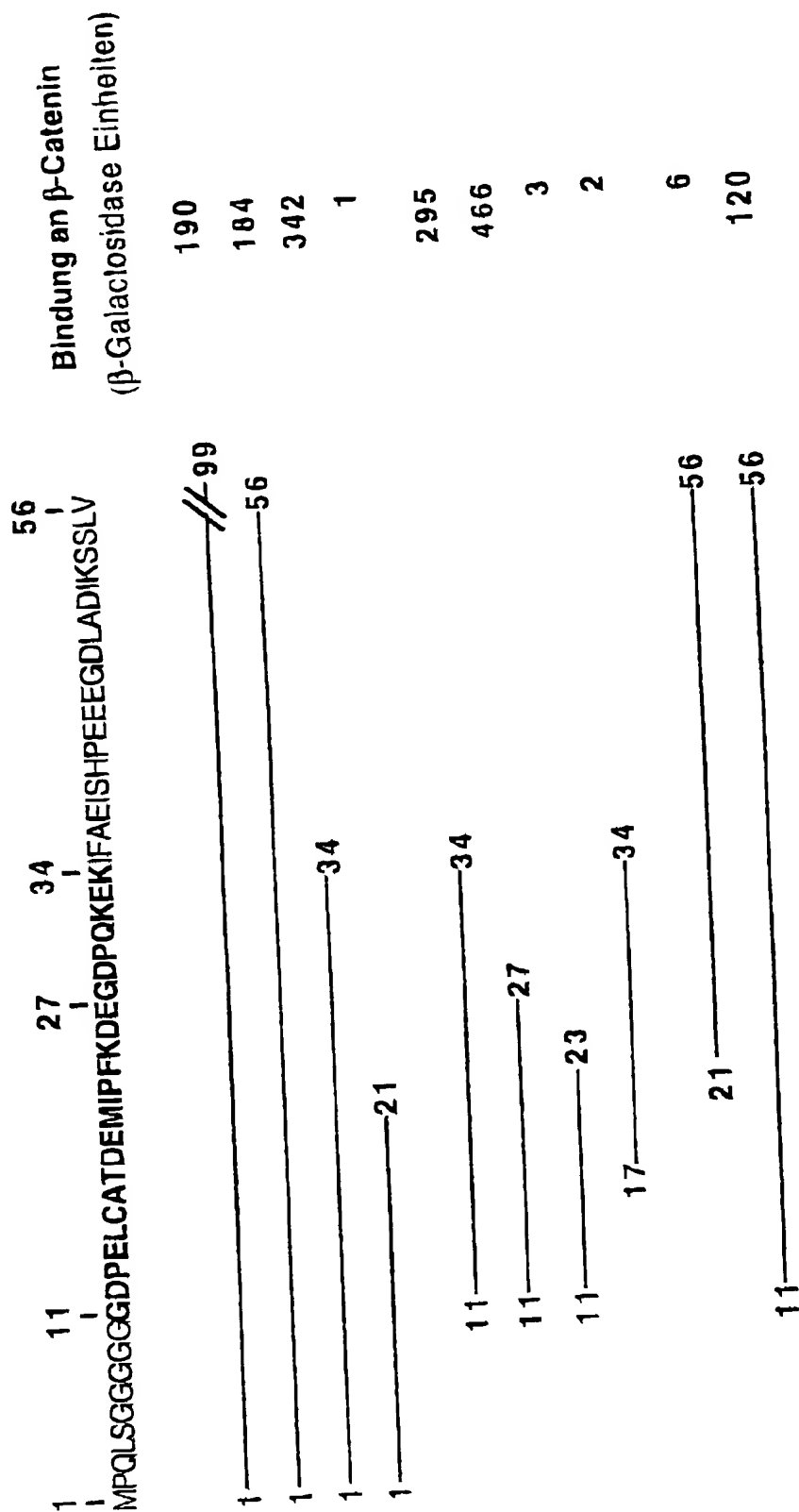


Abb.1

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PCT/DE99/00554

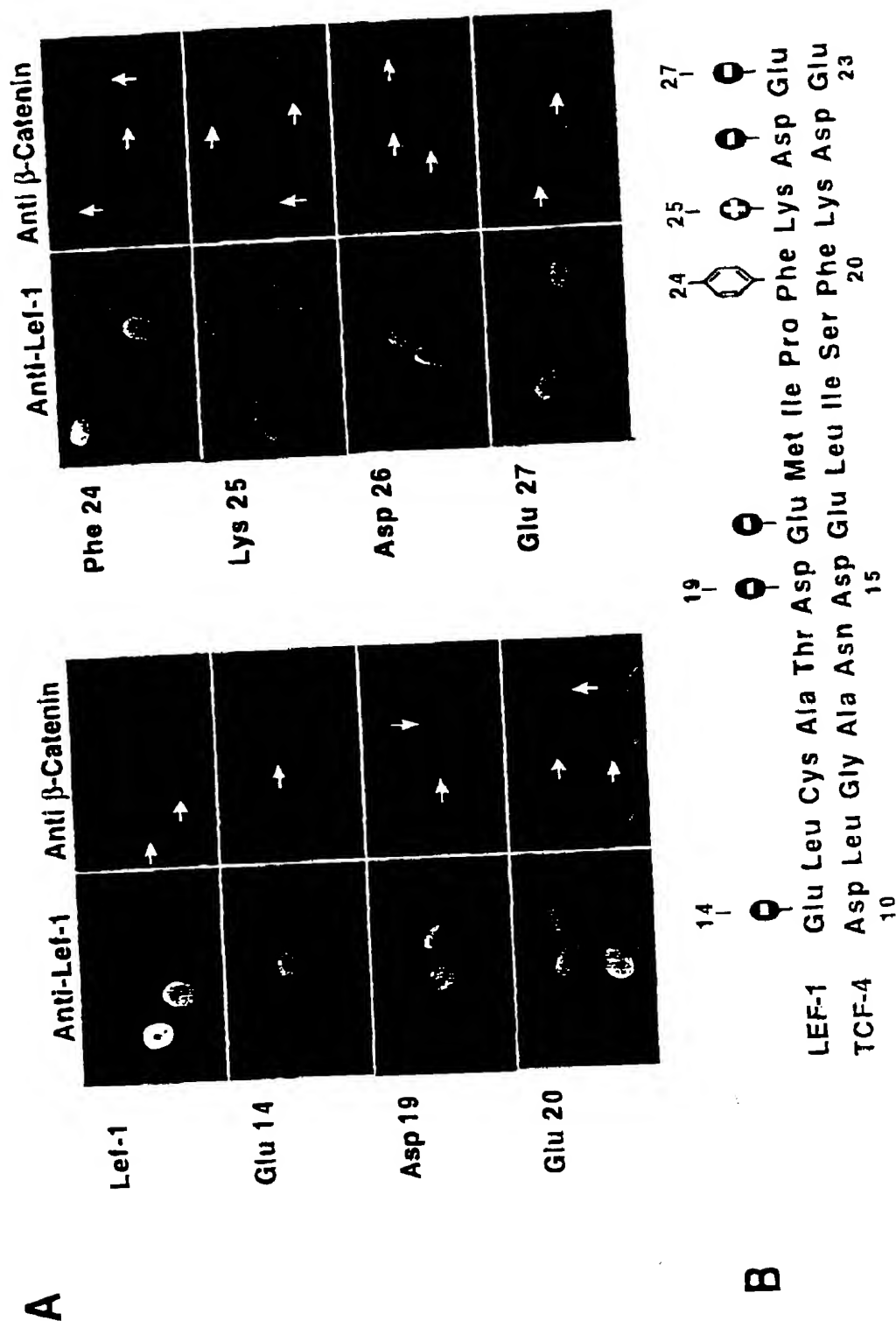


Abb. 4

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PCT/DE99/00554

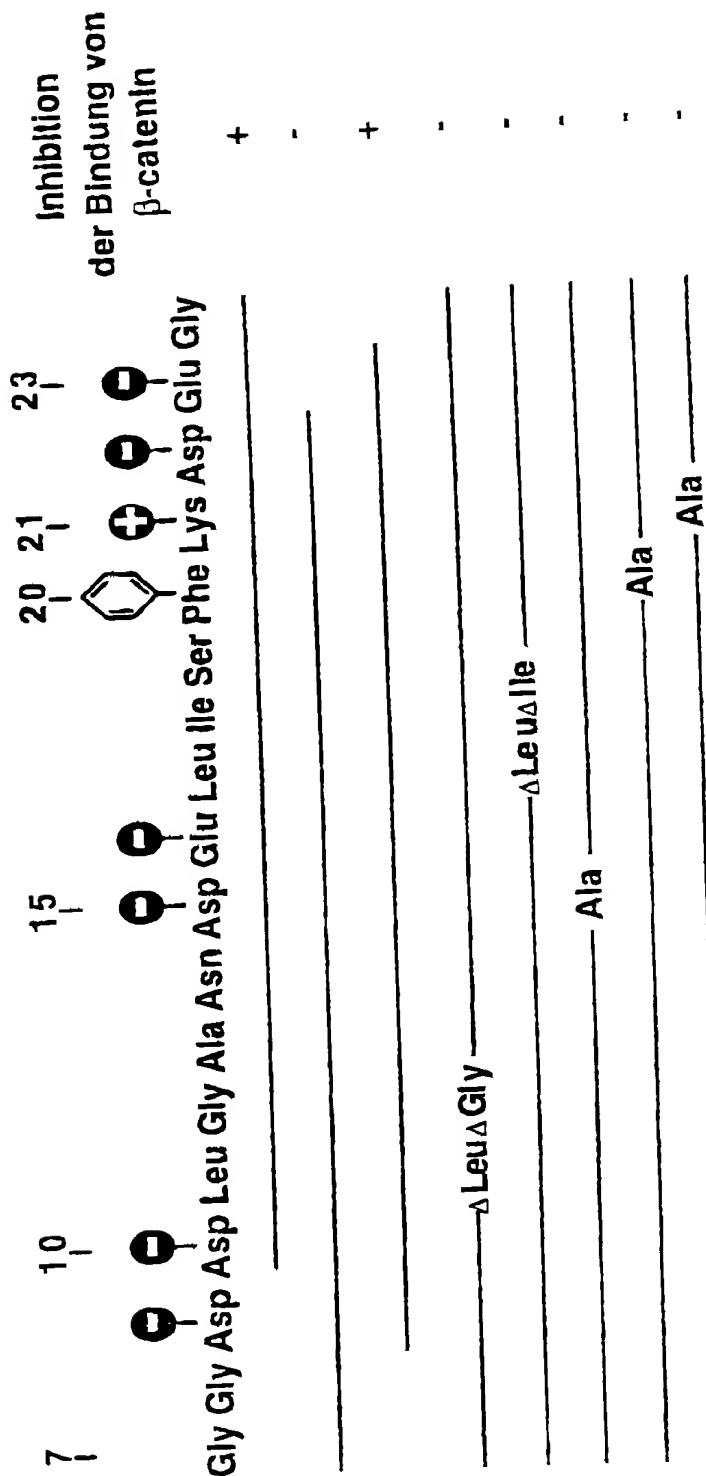


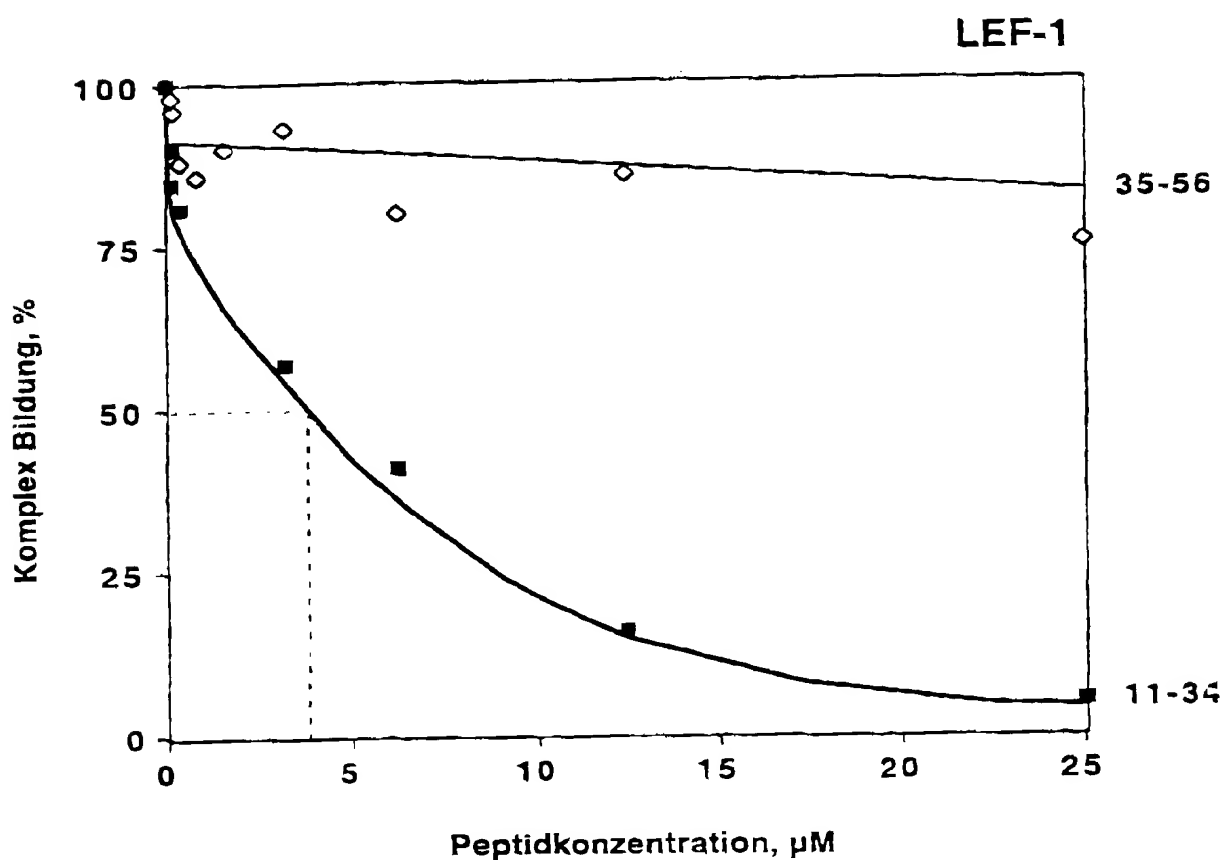
Abb.2

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Inhibition der LEF-1/ β -catenin Interaktion durch synthetische Peptide aus der Minimalen Bindungs-Domäne

**Abb. 3**

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β-Catenin Mutationen mit < 30 % Transaktivierung

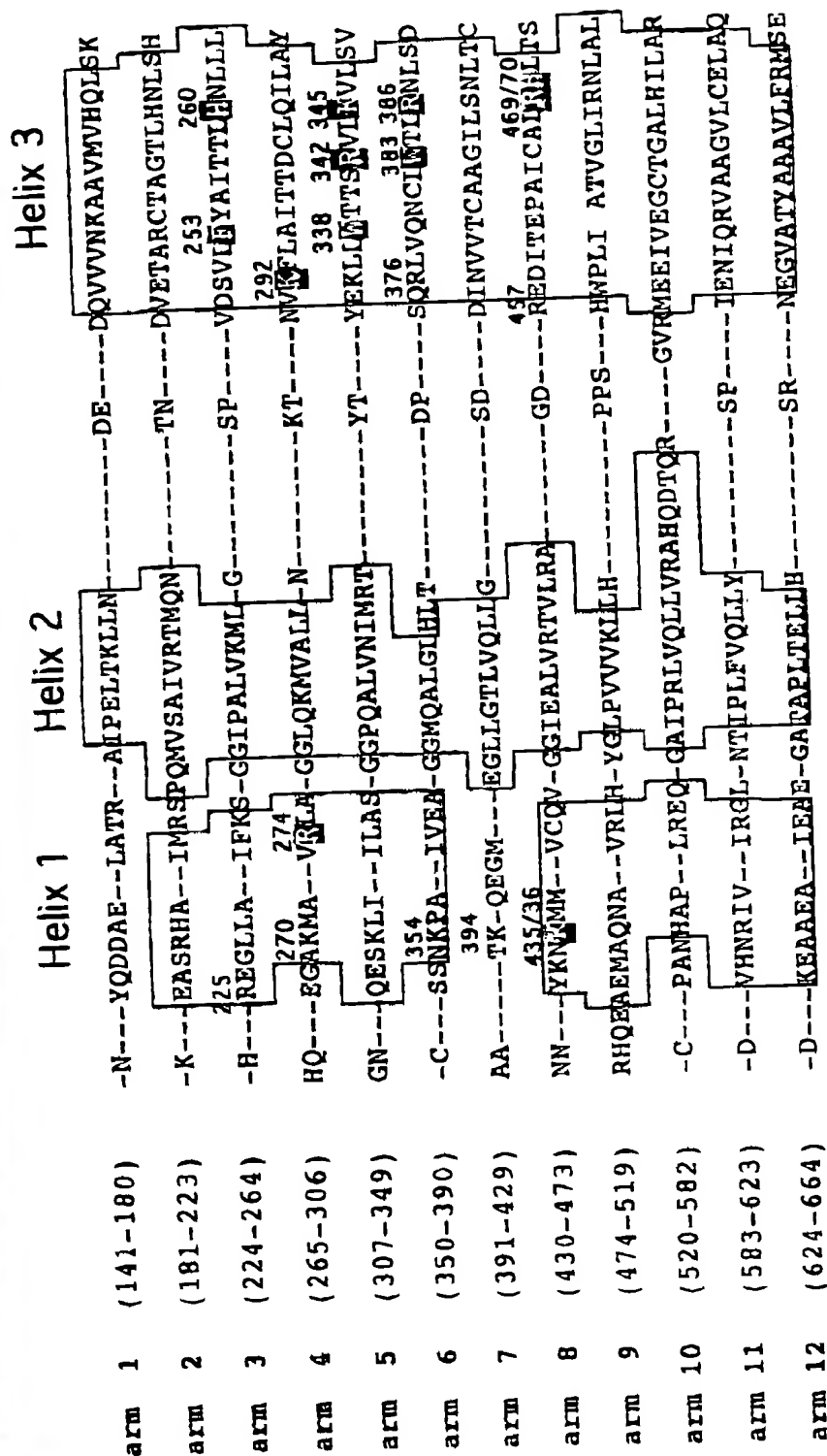


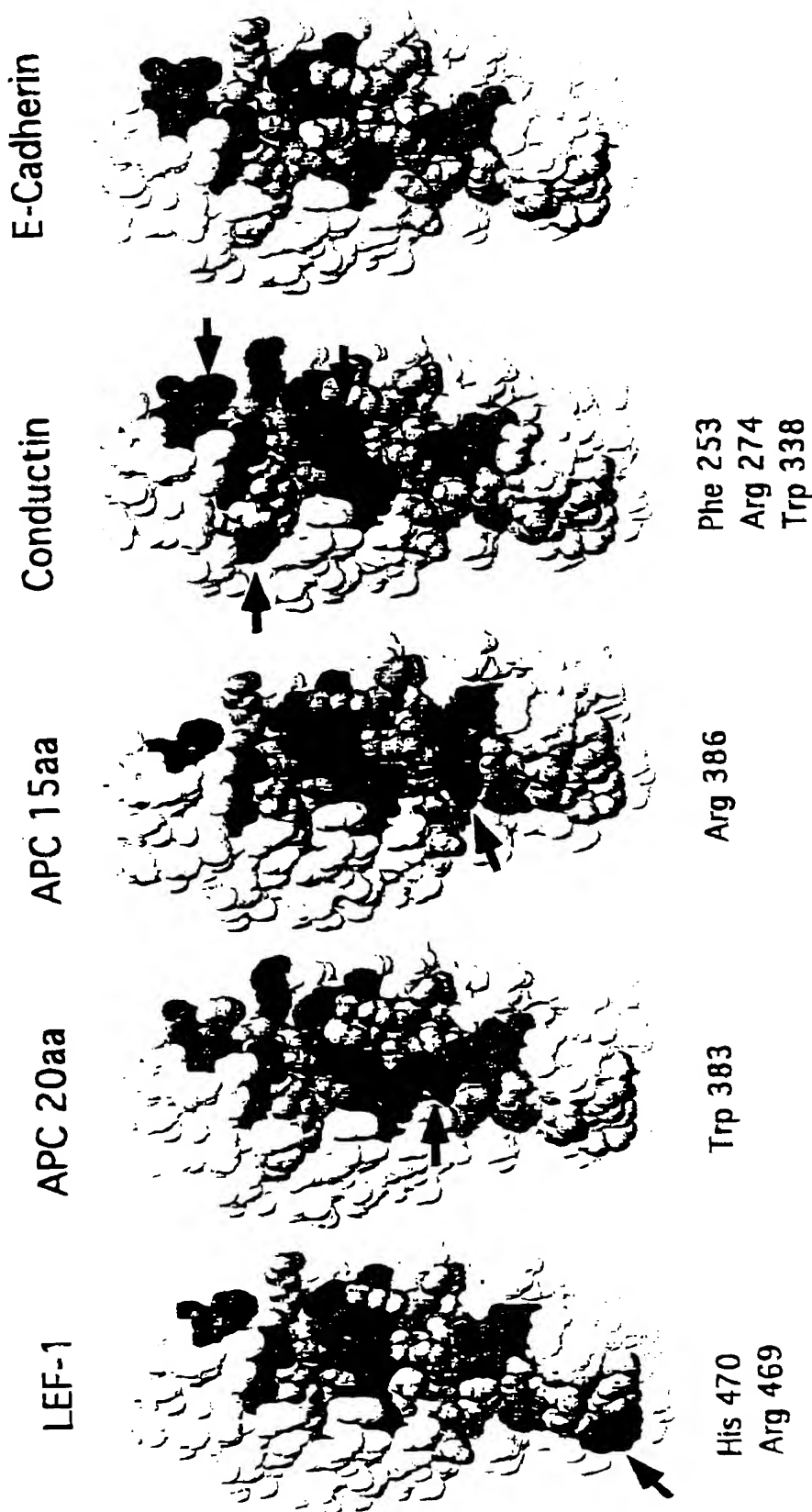
Abb. 5

■ LEF-1
 ■ APC
 ■ Conductin
 E-Cadherin

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Interaktion von β -Catenin Mutanten mit :

Interaktions-Reporteraktivität:

0 - 30 %
30- 60 %

➔ : Mutation für Interaktionspartner spezifisch

Abb. 6

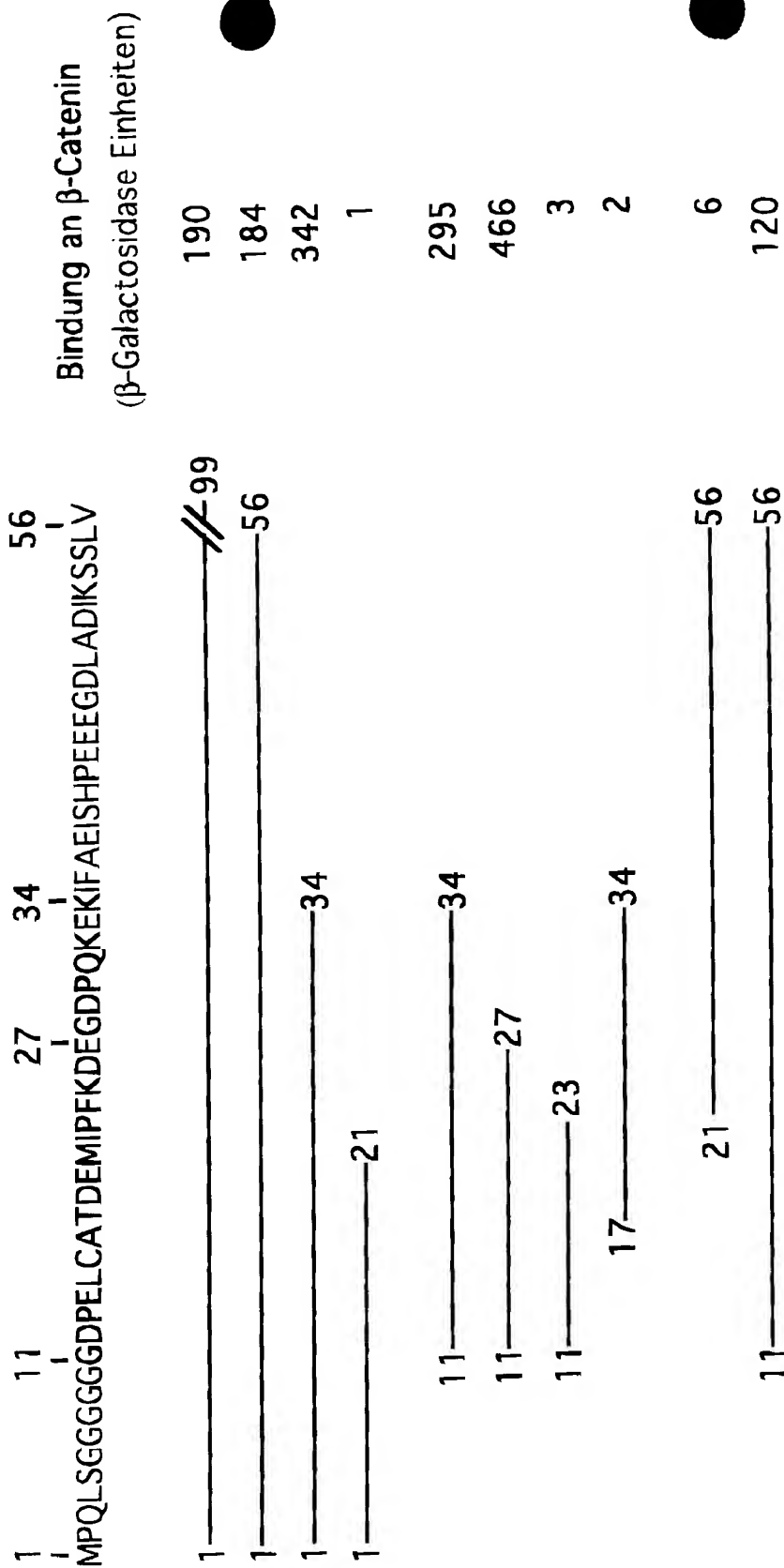


Abb.1

Inhibition der LEF-1/ β -catenin Interaktion durch synthetische Peptide aus der Minimalen Bindungs-Domäne

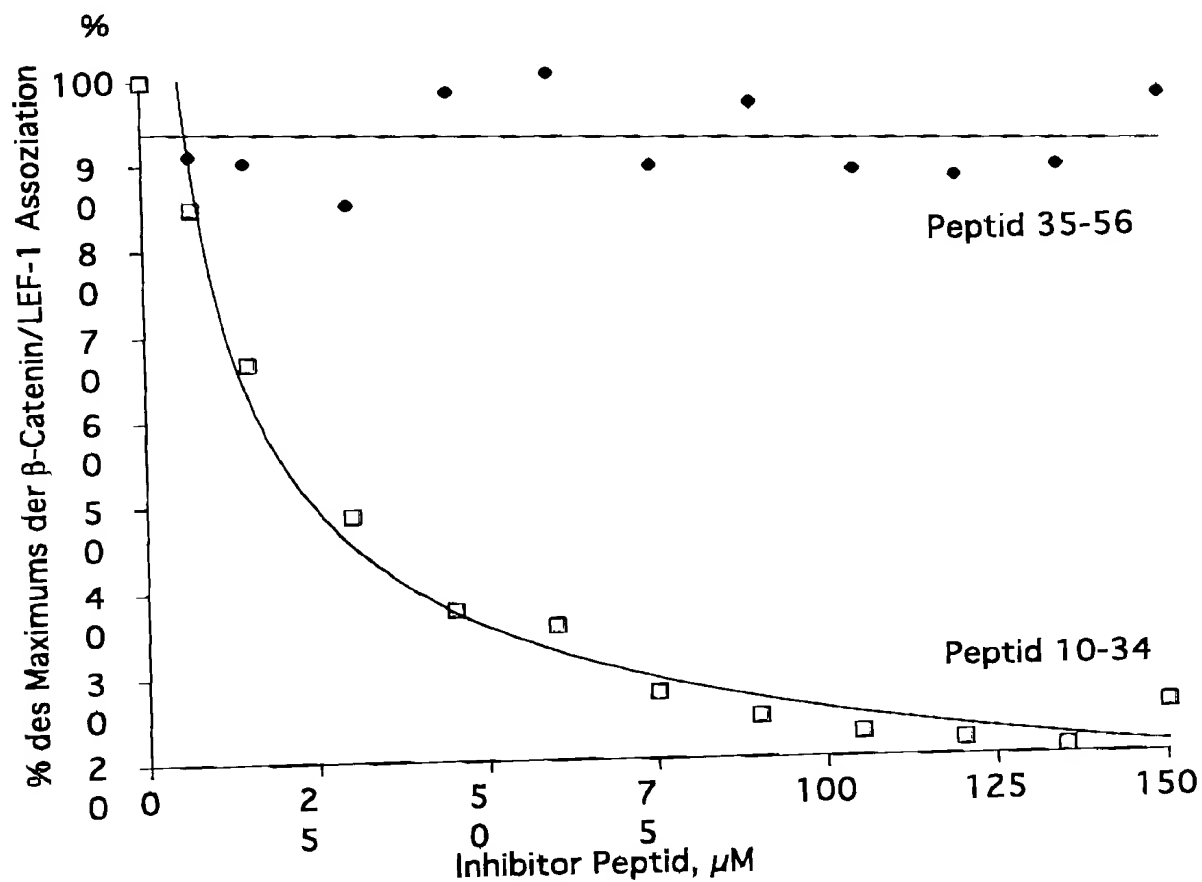
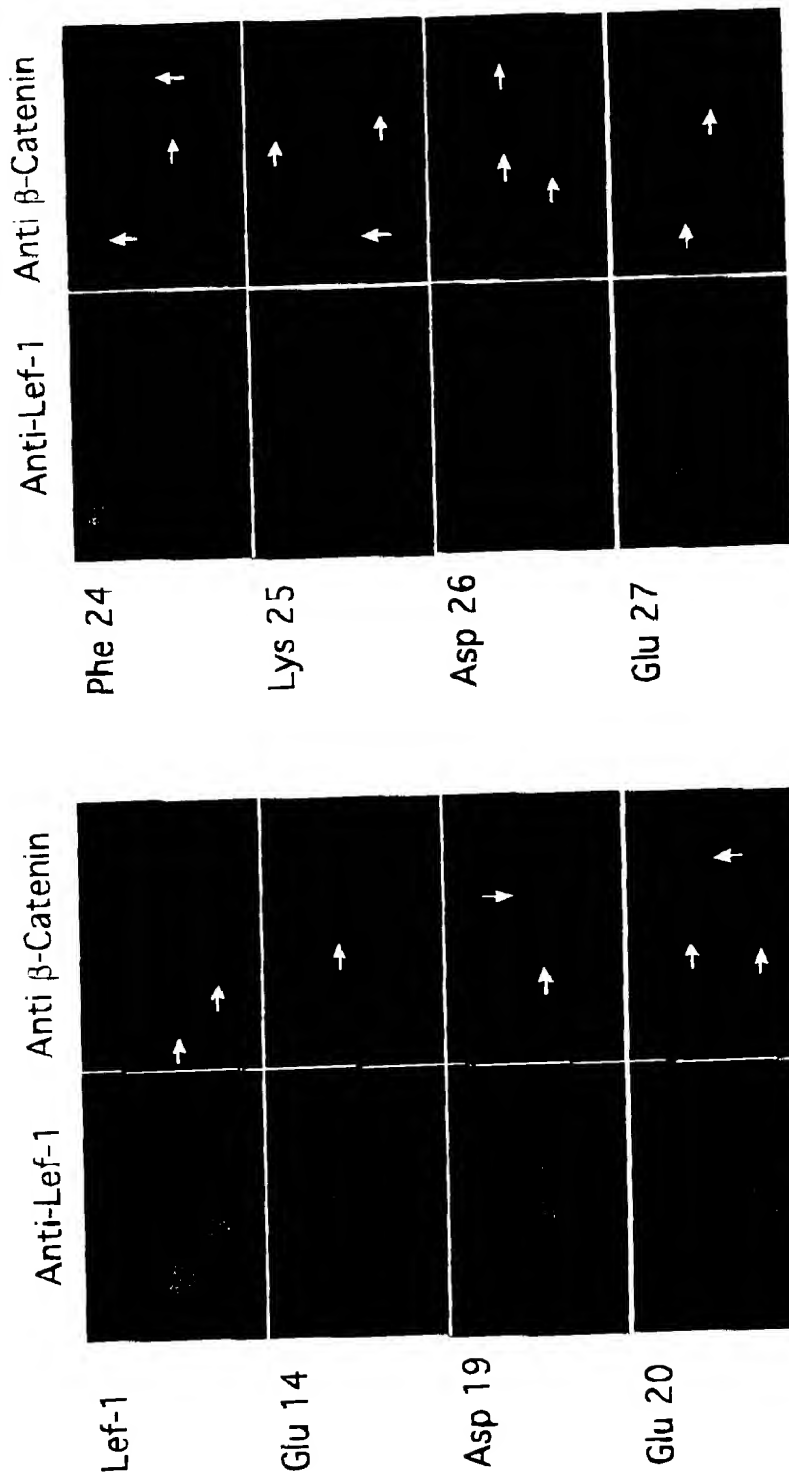


Abb. 3

A



B

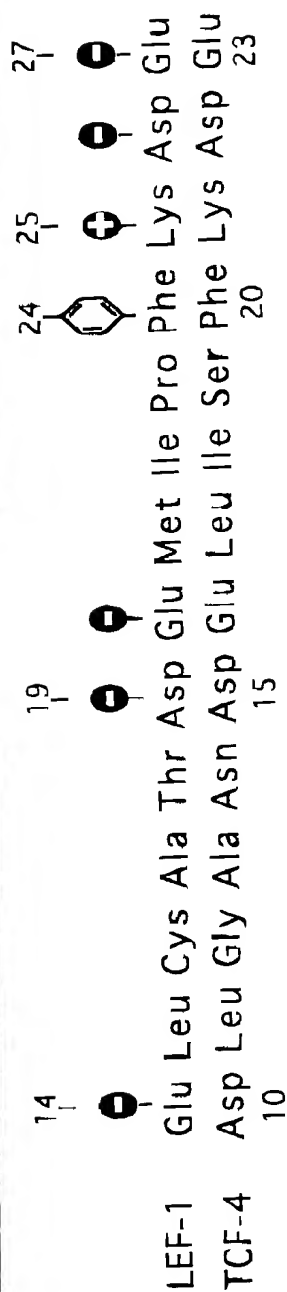


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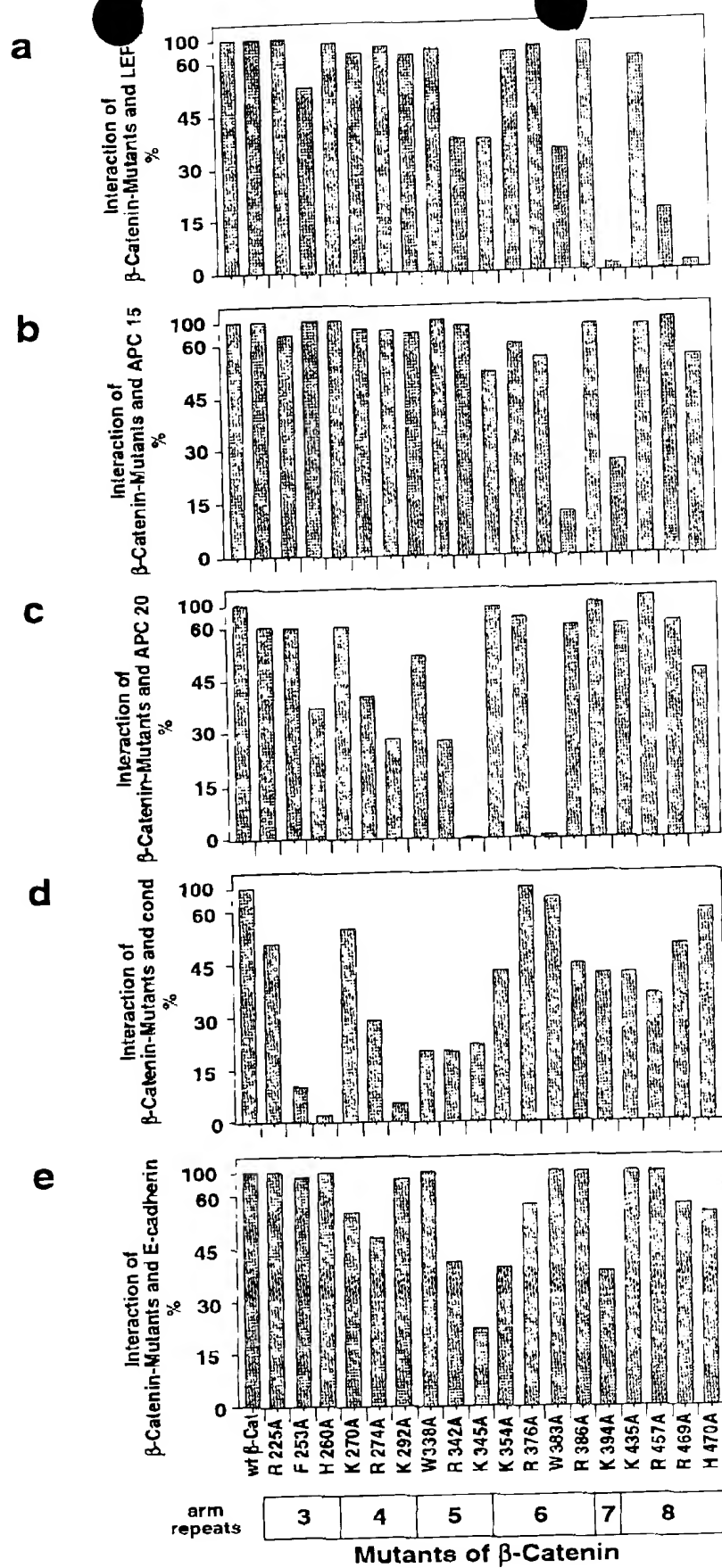


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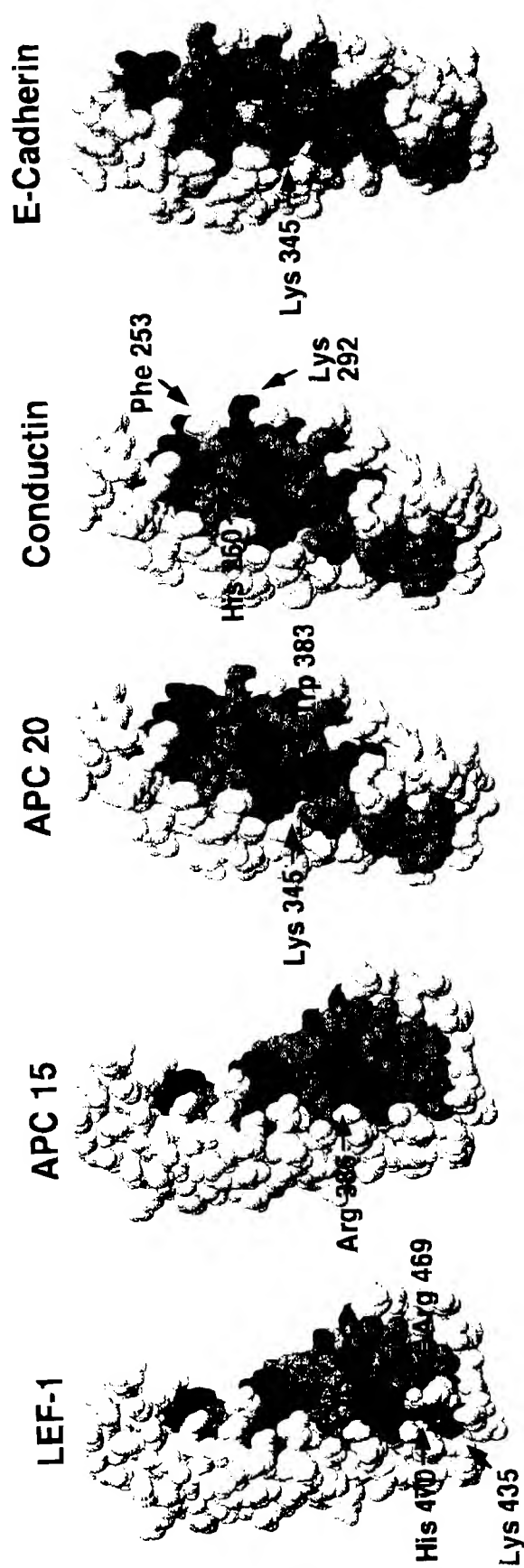


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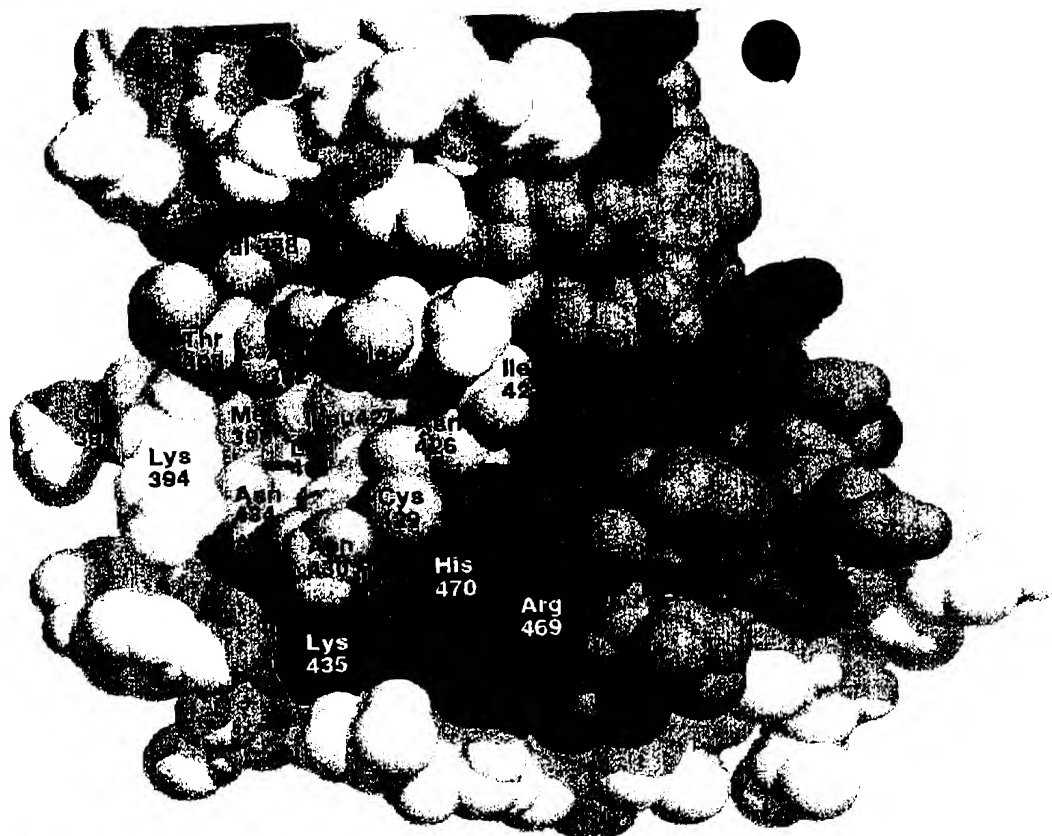
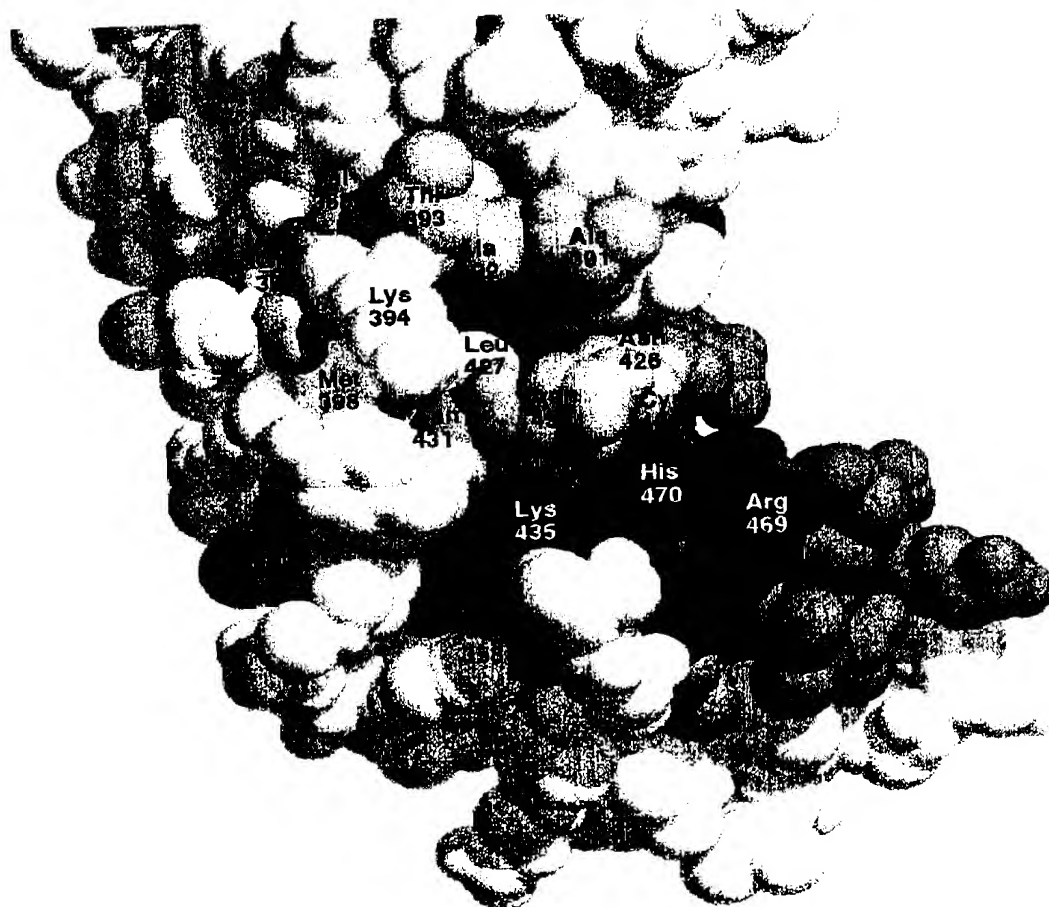
A**B**

Abb. 7

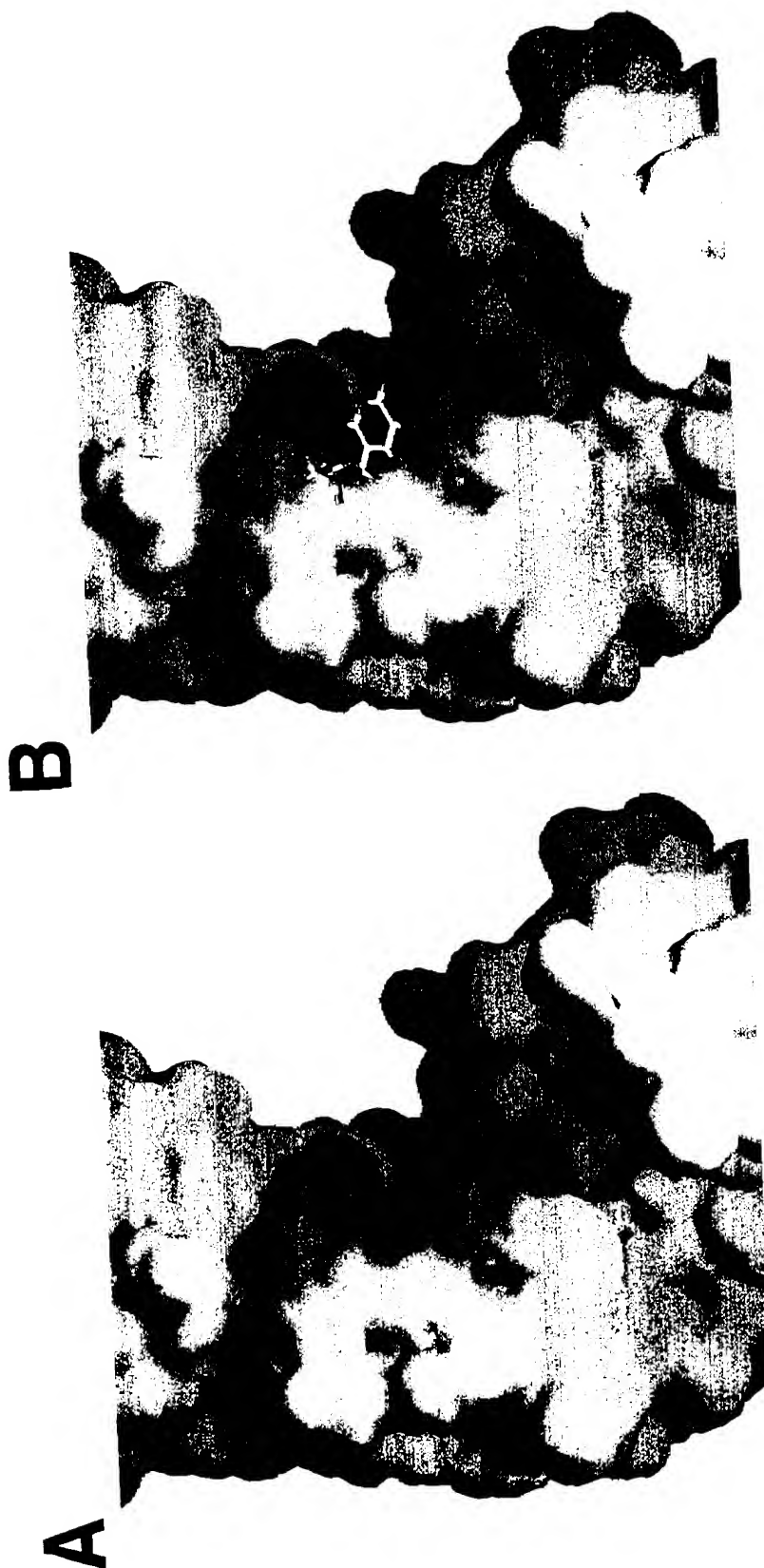
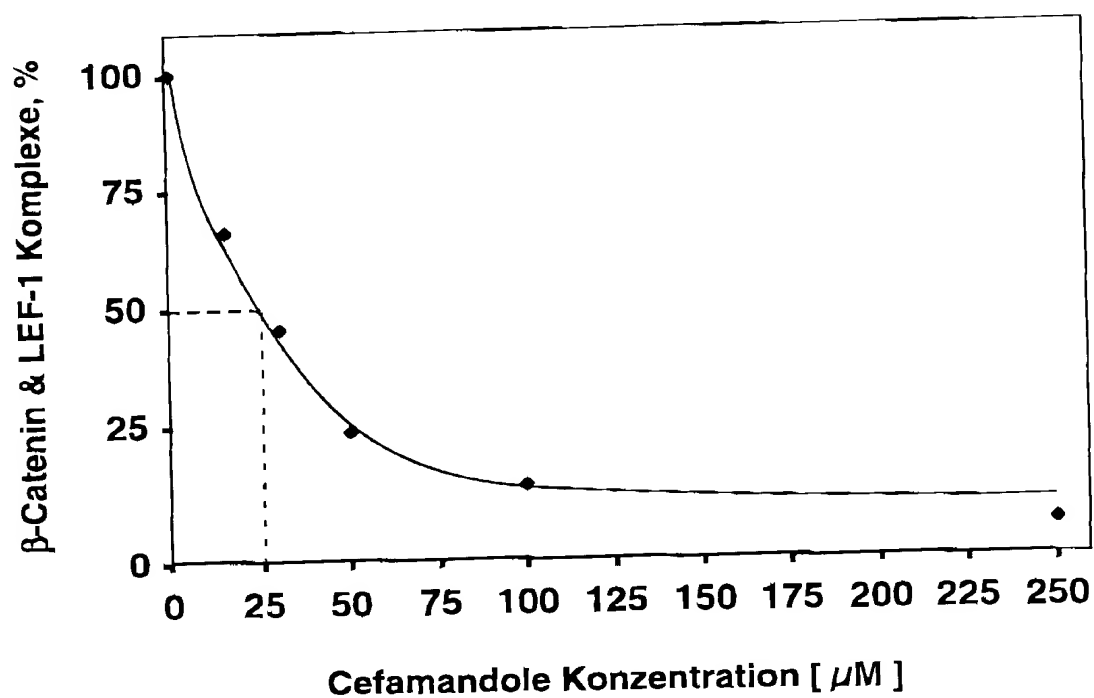


Abb. 8

**Abb. 9**

Tab.1

Aminosäuresequenz des humanen β -Catenin (Armadillo-Repeats 3-9)

arm 3	(224-264)	HR EGLLAIFKSGGPPALVKKMGLGSPVDSVLEFYAITTBNLLSE
arm 4	(265-306)	HQEGA MAVRIAGGLQKMVALLNKTNVKFLAITTBCLQILAY
arm 5	(307-349)	GNQESKLIILASGGPQALVNIMRTYTYEKKLLWTTTSRVLKVLVS
arm 6	(350-390)	CSSNKPATIVEAGMQALGLHLTDPSQRLVQNCLWTLRNLS
arm 7	(391-429)	AATKQEGMEGLLGTLYQLLGSDDINVVTCAAGILSNLTC
arm 8	(430-473)	NNYKNKMMVCEQVGGIEALVRTVLRAGDREDITEPAICALRHLS
arm 9	(474-519)	RH QEAETRAONAVRHHYGLPVVVKLLHPPSHWPLIKATVGLFRNLAL

Tab.2

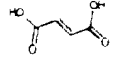
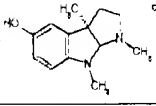
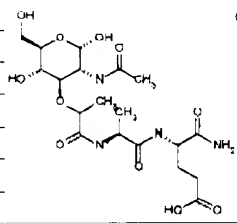
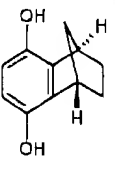
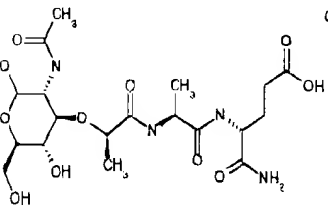
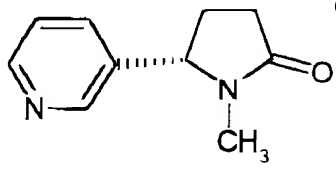
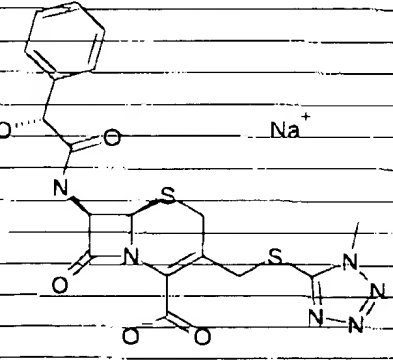
Interaktion von β -Catenin Mutanten mit
LEF-1, APC (20 und 15 Aminosäure -Repeats),
Conductin und E-Cadherin

β -Catenin Mutanten	arm. Einh.	Interaktion mit				
		LEF-1	APC-20	APC-15	Conductin	E-Cadherin
Phe 253	3	-	40	-	17	-
His 260	3	50	40	100	10	100
Arg 274	4	-	40	-	29	50
Lys 292	4	-	28	-	5	-
Trp 338	5	-	55	-	20	-
Arg 342	5	-	29	-	20	41
Lys 345	5	38	0	-	22	27
Lys 354	6	38	-	54	43	40
Trp 383	6	-	0	59	-	-
Arg 386	6	35		12	45	-
Lys 394	7	-	-	-	42	-
Lys 435	8	-	-	30	42	-
Arg 457	8	-	-	-	36	-
Arg 469	8	17	-	-	-	50
His 470	8	2	47	60	-	-

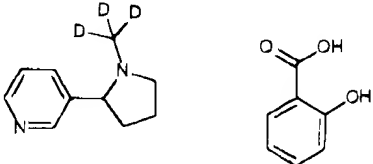
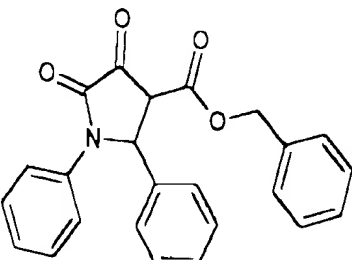
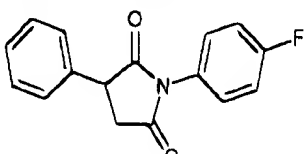
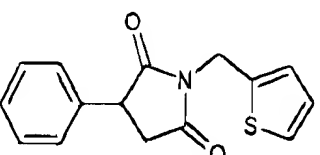
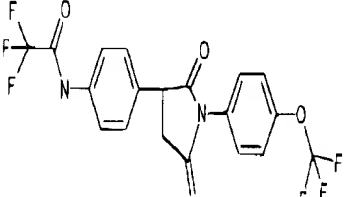
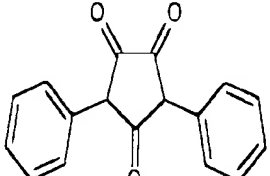
Die Werte geben den prozentualen Anteil der jeweiligen Interaktion im Vergleich zu der mit Wildtyp- β -Catenin an. Durch "-" gekennzeichnete Interaktionen entsprechen , 60 -100 % der Wildtyp-Interaktion.

Tab. 3

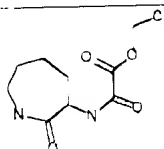
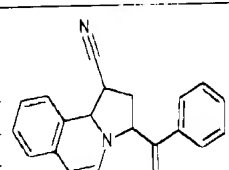
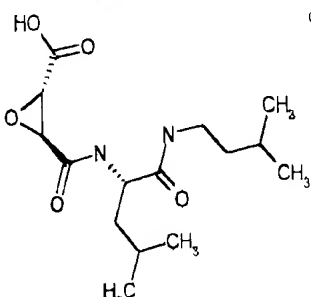
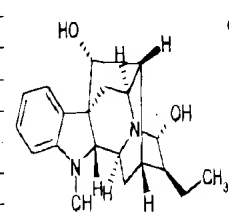
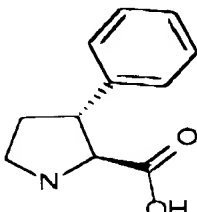
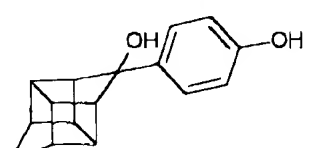
drugs-liste 2000

MOLEKÜLSTRUKTUR	Substanzname	MDL-Nr.
	(-)-ESEROLINE FUMARATE	MFCD00055202
		
	N-ACETYL-MURAMYL-ALA-ISOGLN-OH	MFCD00065478
	3,6-DIHYDROXYBENZONORBORNANE	MFCD00077441
	N-ACETYL-MURAMYL-ALA-D-ISOGLN-OH	MFCD00077638
	(-)-COTININE	MFCD00077696
	CEFAMANDOLE SODIUM SALT	MFCD00082385

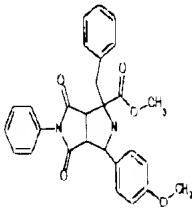
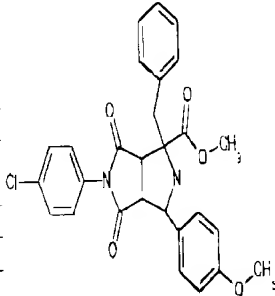
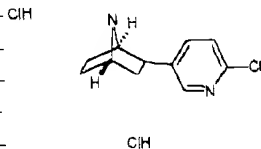
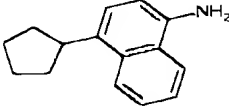
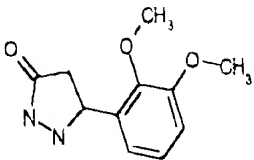
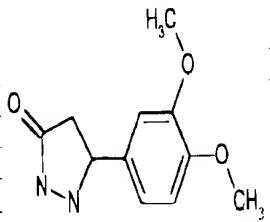
drugs-liste 2000

	(+/-)-NICOTINE-D3 SALICYLATE SALT	MFCD00083448
	BENZYL 1,2-DIPHENYL-4-HYDROXY-5-OXO-3-PYRROLINE-3-CARBOXYLATE	MFCD00088051
	1-(4-FLUOROPHENYL)-3-PHENYLPYRROLIDINE-2,5-DIONE	MFCD00097831
	3-PHENYL-1-(2-THIENYLMETHYL)PYRROLIDINE-2,5-DIONE	MFCD00097832
	N1-(4-[2,5-DIOXO-1-[4-(TRIFLUOROMETHOXY)PHENYL]TETRAHYDRO-1H-PYRROL-3-YL]PHENYL)-2,2,2-TRIFLUOROACETAMIDE	MFCD00100474
	1,3-DIPHENYLCYCLOPENTANE-2,4,5-TRIONE	MFCD00101320

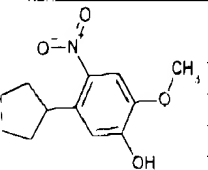
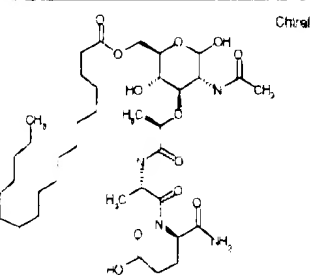
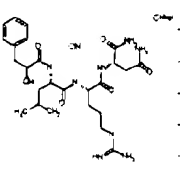
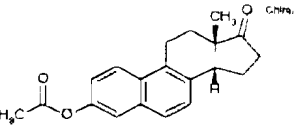
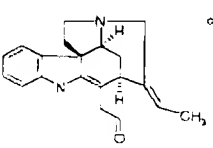
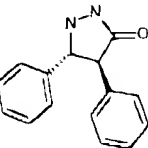
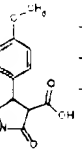
drugs-liste 2000

	ETHYL 2-OXO-2-[(2-OXOAZEPAN-3-YL)AMINO]ACETATE	MFCD00103142
	3-BENZOYL-1,2,3,10B-TETRAHYDRO-PYRROLO(2,1-A)ISOQUINOLINE-1-CARBONITRILE	MFCD00123443
	L-TRANS-EPOXYSUCCINYL-LEU-3-METHYLBUTYLAMIDE	MFCD00132882
	AJMALINE	MFCD00135652
	(2S,3R)-3-PHENYLPYRROLIDINE-2-CARBOXYLIC ACID	MFCD00142984
	4-(2-HYDROXYOCTAHYDRO-1,3,4-METHENO-2H-CYCLOBUTA(CD)PENTALEN-2-YL)PHENOL	MFCD00155174

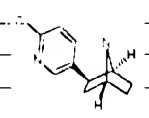
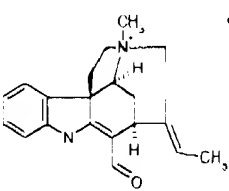
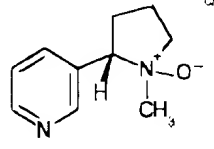
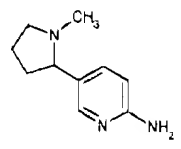
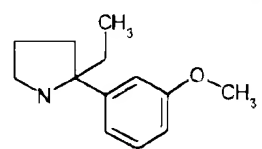
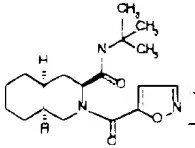
drugs-liste 2000

	METHYL C-4-(4-METHOXYPHENYL)-2-BENZYL-7-PHENYL-6,8-DIOXO-3,7-DIAZABICYCLO[3.3.0]-OCTANE-R-2-CARBOXYLATE	MFCD00202518
	METHYL C-4-(4-METHOXYPHENYL)-2-BENZYL-7-(4-CHLOROPHENYL)-6,8-DIOXO-3,7-DIAZABICYCLO[3.3.0]-OCTANE-R-2-CARBOXYLATE	MFCD00202519
	(+/-)-EPIBATIDINE DIHYDROCHLORIDE	MFCD00210196
	4-CYCLOPENTYL-NAPHTHALEN-1-YLAMINE, HYDROCHLORIDE	MFCD00227852
	5-(2,3-DIMETHOXY-PHENYL)-PYRAZOLIDIN-3-ONE	MFCD00228403
	5-(3,4-DIMETHOXY-PHENYL)-PYRAZOLIDIN-3-ONE	MFCD00229211

drugs-liste 2000

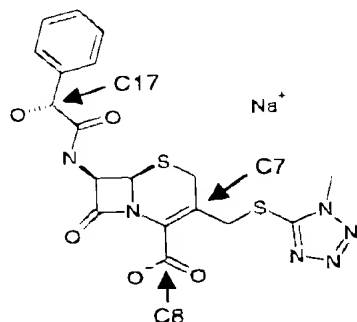
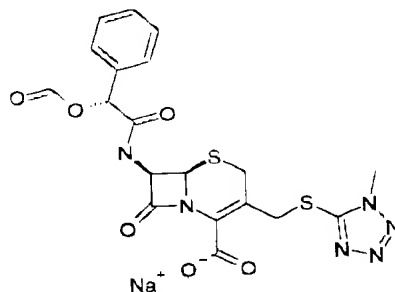
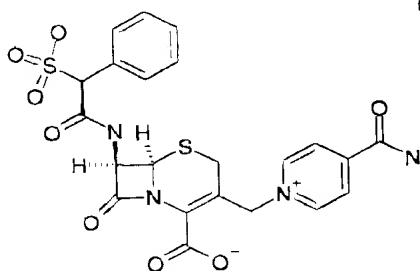
	5-CYCLOPENTYL-2-METHOXY-4-NITRO-PHENOL	MFCD00230901
	AC-(6-O-STEARYL)-MURAMYL-ALA-D-ISOGLUTAMINE	MFCD00236777
	ANTHO-RNAMIDE	MFCD00236789
	1,3,5(10),6,8(14)-ESTRAPENTAEN-3-OL-17-ONE ACETATE	MFCD00271642
	NORFLUOROCURARINE	MFCD00274483
	4,5-DIPHENYLPYRAZOLIDIN-3-ONE	MFCD00277796
	4-(4-METHOXY-PHENYL)-2-OXO-PYRROLIDINE-3-CARBOXYLIC ACID	MFCD00297824

drugs-liste 2000

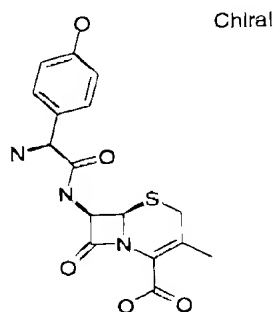
	Cl ⁻	(+)-EPIBATIDINE HYDROCHLORIDE	MFCD00467208
	Cl ⁻	FLUOROCURARINE CHLORIDE	MFCD00467712
		(1'S,2'S)-NICOTINE 1'-OXIDE	MFCD00869528
	ClH	SPECS SPECS CIF7952	MFCD01114864
		2-ETHYL-2-(3-METHOXYPHENYL)PYRROLIDINE	MFCD01314146
		N-(TERT-BUTYL)-2-(ISOXAZOL-5-YLCARBONYL)DECAHYDROISOQUINOLINE-3-CARBOXAMIDE	MFCD01314517

Tab. 4

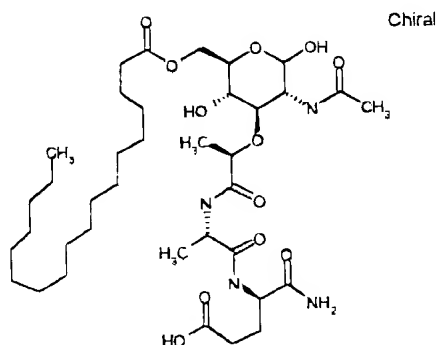
Positiv-Liste

Molekül-Klasse IA (Inhibitoren vom Cefamandole-Typ)**Cefamandole****Cefamandole-Nafate**

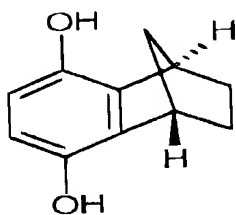
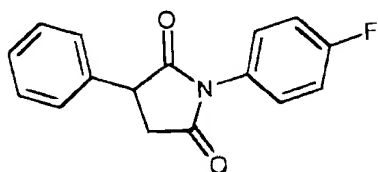
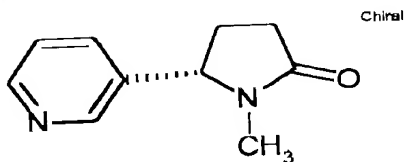
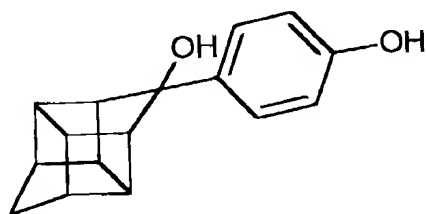
Chiral

Cefsulodin

Chiral

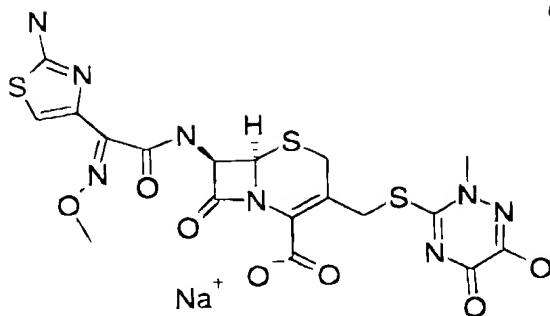
Cefadroxil**Molekül-Klasse IB****AC-(6-O-STEAROYL)-MURAMYL-ALA-D-ISOGLUTAMINE**

Positiv-Liste

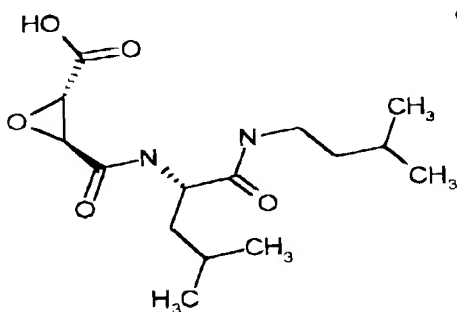
Molekül-Klasse IC**3,6-DIHYDROXYBENZONORBORNANE****Moleküle mit Modulationswirkung für Molekülklasse I****1-(4-FLUOROPHENYL)-3-PHENYLPYRROLIDINE-2,5-DIONE****(-)-COTININE****4-(2-HYDROXYOCTAHYDRO-1,3,4-METHENO-2H-CYCLOBUTA(CD)PENTALEN-2-YL)PHENOL**

Positiv-Liste

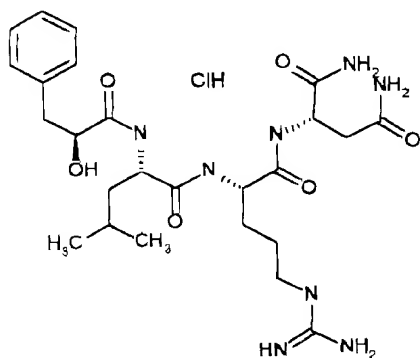
Chiral

**Ceftriaxone**

Chiral

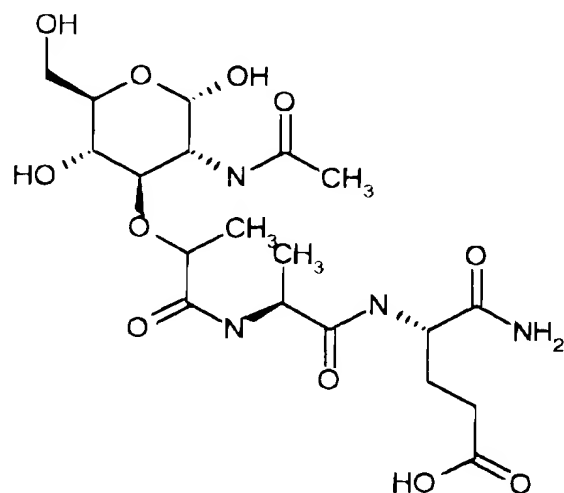
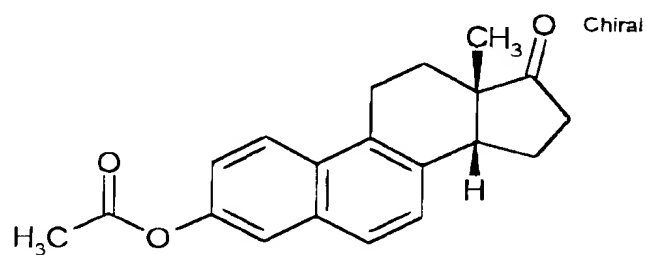
**L-TRANS-EPOXYSUCCINYL-LEU-3-METHYLBUTYLAMIDE**

Chiral

**ANTHO-RNAMIDE**

Positiv-Liste

Chiral

**N-ACETYL-MURAMYL-ALA-ISOGLN-OH****1,3,5(10),6,8(14BETA)-ESTRAPENTAEN-3-OL-17-ONE ACETATE**